IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

	)	**REDACTED PUBLIC VERSION**
IN RE: '318 PATENT INFRINGEMENT LITIGATION	)	Civil Action No. 05-356-SLR
	)	(consolidated)
	)	
	)	

PLAINTIFFS' REPLY BRIEF ON CLAIM CONSTRUCTION

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I. PRELIMINARY STATEMENT AND SUMMARY OF ARGUMENT

Straining to avoid the claim constructions compelled by the unambiguous language of the '318 Patent and confirmed by its file history, Defendants' Opening Claim Construction Brief (hereinafter, "Defendants' Brief" or "Def. Br.") ignores or distorts dispositive intrinsic evidence, misrepresents the extrinsic evidence, and misapplies the law of claim construction. Such tactics do not justify a departure from the proposed constructions set forth in Plaintiffs' portion of the JCCC.

Defendants begin their brief with a "Background" section that is in reality an overview of their misguided invalidity case (which Plaintiffs will not rebut here). However, as the Court knows, the task at hand is not to determine whether Defendants meet their clear and convincing evidentiary burden to prove patent invalidity, but simply to determine what the claims *mean*. Determinations of infringement (conceded here by Defendants) and validity flow from claim construction, not vice versa. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 997 n.7 (Fed. Cir. 1995) (*en banc*), *aff'd*, 517 U.S. 370 (1996).

Despite their oft-intoned mantra that the '318 Patent claims "should be construed to have their ordinary meaning" (Def. Br. at 1), Defendants twice fail to shed any light on what meaning they *do* ascribe to the disputed claim terms, "Alzheimer's disease and related dementias" and "therapeutically effective amount."[1] Defendants' approach provides no guidance

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[1] Defendants imply that Plaintiffs agree with Defendants' definition of a person of ordinary skill. Def. Br. at n. 2. Defendants misstate Plaintiffs' position. The parties' experts *do* disagree as to the level of ordinary skill, and Plaintiffs' experts have opined that Defendants' experts have overstated it. *See, e.g.*, Second Expert Report of Dr. Joseph T. Coyle at ¶¶ 8-10 (Ex. J); Second Expert Report of Dr. Jeffrey L. Cummings at ¶¶ 11-14 (Ex. K); Second Expert Report of Dr. Howard M. Fillit at ¶¶ 8-9 (Ex. L); Second Expert Report of Dr. Murray A. Raskind at ¶¶ 6-8 (Ex. M). Plaintiffs' experts simply conclude that the '318 Patent is valid under (continued...)

to the Court in its task of rendering a clear and definitive interpretation of the '318 Patent, and thus undermines the very purpose of the claim construction process. *AstraZeneca AB v. Mutual Pharm. Co., Inc.*, 384 F.3d 1333, 1336 (Fed. Cir. 2004) ("It is axiomatic that the claims mark the outer boundaries of the patent right to exclude. The critical challenge is to determine the meaning of the claims, *i.e.*, their scope."). For the claim terms that Defendants *do* define, their proposed constructions conflict with the intrinsic evidence and their own experts' opinions.

Moreover, Defendants' brief consistently ignores the context of Dr. Davis's invention directed to a method of treating Alzheimer's disease, despite their recognition that the Court should construe the disputed claim terms by considering the context in which the terms are used. Def. Br. at 5 (citing *Phillips v AHW Corp.*, 415 F.3d 1303, 1314-15 (Fed. Cir. 2005)). For instance, Defendants' flawed definition of "a patient" as including any mammal (Def. Br. at 15-17) ignores the fact that the "mammal" would have to suffer from Alzheimer's disease because the claimed method is of treating Alzheimer's disease. Thus, Defendants' constructions are divorced from the context of the '318 Patent.

Accordingly, for the reasons set forth in Plaintiffs' Opening Brief and below, the Court should adopt Plaintiffs' proposed constructions set forth in the JCCC.

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either standard. The question whether the level of skill affects claim construction has not been joined because Defendants' experts did not opine on claim construction issues in their reports.

II. DISCUSSION OF DISPUTED TERMS

A. "Alzheimer's Disease and Related Dementias"

It is undisputed that as used in the '318 Patent, "Alzheimer's disease and related dementias" includes at least presenile dementia. The parties disagree, however, about what "related dementias" means in the context of the '318 Patent.[2]

Relying upon the intrinsic evidence, Plaintiffs contend that the term "Alzheimer's disease and related dementias" must include not only the rare, presenile form of Alzheimer's disease seen in younger patients, but also senile dementia of the Alzheimer's type – the far more prevalent condition among the elderly. Plaintiffs' Opening Brief on Claim Construction (hereinafter, "Plaintiffs' Brief" or "Pl. Br.") at 7-9. Defendants dispute this interpretation, yet they fail to offer a competing meaning of the term. Instead, their definition is circular, and does not provide any guidance to the Court as to what "Alzheimer's disease and related dementias" means. Specifically, Defendants ask this Court to define the "related dementias" to mean "dementias related to Alzheimer's disease," JCCC at 1, which sheds no light on the claim term.

Defendants' elaboration on the "meaning" of this term (disclosed for the first time in their Opening Brief) only further illustrates the flaw in their approach. They provide an open-ended list of diseases that share dementia as a symptom, even though they have no pathophysiological commonality with Alzheimer's disease. Defendants contend that these unrelated diseases are "*[a]mong* the dementias that were viewed as being related to Alzheimer's

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[2] The parties appear to agree that although the term "Alzheimer's disease and related dementias" appears in the claim preamble, it serves as an antecedent basis for other disputed claim terms and thus serves to limit the claim. *See Rapoport v. Dement*, 254 F.3d 1053, 1059 (Fed. Cir. 2001).

disease in 1986." Def. Br. at 9 (emphasis added).[3] Such a non-exhaustive list is not helpful to the Court and appears aimed at preserving flexibility for Defendants to later argue that "related dementias" covers other disorders.

Moreover, claim terms should define the metes and bounds of the patented invention. *See* 35 U.S.C. § 112 ("The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention."). Therefore, as between an interpretation of a claim term that is potentially open-ended and one that is finite, the Court should choose the latter. *See Modine Mfg. Co. v. United States Int'l Trade Comm'n*, 75 F.3d 1545, 1556 (Fed. Cir. 1996) (claims amenable to multiple constructions should be interpreted to preserve their validity).

In addition, Defendants' construction finds no support in the intrinsic evidence. Defendants only once cite intrinsic evidence relating to this term, and the passage cited refers to the inclusion of presenile dementia, which is undisputed. *See* Def. Br. at 7-9.[4]

This is unsurprising because the intrinsic evidence supports Plaintiffs' construction. As noted in Plaintiffs' Brief (at 8-9), Dr. Davis disclosed to the PTO a July 1986 article by Hershenson and Moos, "Drug Development for Senile Cognitive Decline," Journal of Medicinal Chemistry, 29(7):1125-1130 (hereinafter "the Hershenson article," Pl. Br. at Ex. F).

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[3] Defendants also state that their laundry list of dementias that were allegedly understood in 1986 to be dementias related to Alzheimer's disease "*included, but were not limited to* senile dementia of the Alzheimer's type" and nine different diseases. Def. Br. at 9 (emphasis added).

[4] In the JCCC, Defendants do not identify which cites to the '318 Patent support their definition of "related dementias" (as distinct from "Alzheimer's disease"), nor could they. JCCC at 1. Defendants' three citations (Pl. Br. at Ex. A, '318 Patent at 1:34-36, 1:45-46, and claim 1) refer either to the undisputed inclusion of presenile dementia, or to the disputed claim language. Not one of the many diseases identified in Defendants' Brief is mentioned.

The Hershenson article identified the various names that were used to describe Alzheimer's disease in 1986, stating, in relevant part:

> Currently, several dementias can be treated ... but others cannot, most notably primary degenerative dementia (PDD); also called senile dementia, senile dementia of the Alzheimer's type, Alzheimer's disease, organic brain syndrome.

Id. at 1125 (SYN-RAZ 003460). By directing attention to these conditions, Dr. Davis informed the patent examiner precisely what she understood were "dementias" (plural) "related" to Alzheimer's disease. Accordingly, Defendants' claims that Plaintiffs "cannot identify [support for their construction] anywhere in the ... prosecution history" and that Plaintiffs' construction "cannot be supported by the syntax of the claim" ring hollow. Def. Br. at 7-8.

Moreover, during prosecution, Dr. Davis distinguished her invention from efforts to treat conditions that share symptoms with Alzheimer's disease by noting that cognitive impairment in Alzheimer's disease stems from a different physiological source (i.e., nerve cell degeneration, neural pathway damage, and neurofibrillary tangles). In responding to claim rejections based on publications concerning memory enhancement in animals having conditions with different neuropathologies from Alzheimer's disease, Dr. Davis stated:

> It is true that in Alzheimer's disease there is memory loss. However this is apparently *associated with physiological changes in the brain including degeneration of nerve cells in the frontal and temporal lobes, damage in the neural pathways to the hippocampus and the creation of neurofibrillary tangles in nerve cells*. . . . To say simply that because a particular drug has some effect on a symptom caused by one underlying condition, it will have a useful effect on another underlying condition is clearly wrong.

Pl. Br. at Ex. G. at 3-4 (emphasis added). Here, Defendants seek a definition of "related dementias" that ignores this context. Plaintiffs submit that the distinction drawn by Dr. Davis between conditions that share symptoms (e.g., memory loss) with Alzheimer's disease and those that share its neuropathology – clear from the intrinsic record – limits "related dementias" to

those having a common physiology, namely, to the synonyms identified in the Hershenson article above.[5]

Although the Court need not consider any extrinsic evidence in view of the intrinsic evidence described above,[6] the extrinsic evidence properly before the Court does not advance Defendants' position. As an initial matter, this Court should not consider the opinions of Dr. Levey offered for the first time during his deposition (after the parties exchanged proposed claim constructions) on the meaning of "related dementias." Def. Br. at 9. As Dr. Levey conceded, **REDACTED** .[7] *See* Ex. N, Levey Dep. at 220:14-221:7. As the Federal Rules of Civil Procedure make clear, expert reports must contain "*a complete statement of all opinions* to be expressed and the bases and reasons therefor...." Fed. R. Civ. P. 26(a)(2)(B) (emphasis added). Dr. Levey's belated attempt to offer an opinion on "related dementias" at his deposition should be rejected. *See* Fed. R. Civ. P. 37(c)(1); *see also, e.g., 02 Micro Int'l Ltd. v. Monolithic Power Sys., Inc.*, 467 F.3d 1355, 1368-69 (Fed. Cir. 2006) (excluding evidence pertaining to theory not disclosed in expert report).[8]

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[5] Notably, Dr. Davis distinguished her invention from potential treatment of Wernike-Korsakoff Syndrome – which is one of the unrelated diseases that Defendants lump into their definition of "related dementias." Def. Br. at 9. The '318 Patent file history thus expressly reveals that this disease is *not* a related dementia to Alzheimer's disease.

[6] As the Defendants acknowledge, "extrinsic evidence should be disregarded where it is 'clearly at odds with the claim construction mandated by the claims themselves ... [and] the written record of the patent." Def. Br. at 6 (quoting *Phillips*, 415 F.3d at 1318, 1320-24).

[7] In fact, neither of Defendants' medical experts ever offered *any* opinion prior to deposition on the construction of "Alzheimer's disease and related dementias" or any other disputed claim term.

[8] **REDACTED**
Def. Br. at Ex. 4.

In any event, Dr. Levey's undisclosed opinion is contradicted by the deposition testimony of Defendants' other medical expert, Dr. Domino, who testified

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See Ex. O, Domino Dep. at 211:9-213:14.

With respect to the testimony of Plaintiffs' expert, Dr. Jeffrey Cummings, Defendants are incorrect that "[w]hen asked what dementias were viewed as related to Alzheimer's disease as of 1986, [Dr. Cummings] provided nearly the same list as Dr. Levey." Def. Br. at 9. Defendants' brief takes Dr. Cummings's testimony out of context by quoting his response to the question, "from a *clinical perspective*, as of 1986 what dementias were viewed as being related to Alzheimer's disease?" without identifying his "clinical perspective" as a qualification on the question and answer. Dr. Cummings's testimony is clear that from a *neuropathological perspective* – the proper perspective identified by Dr. Davis during prosecution – the only "related dementias" pertinent here are Alzheimer's disease and senile dementia. *See* Ex. P, Cummings Dep. at 135:14-136:3 ("Q: [O]ther than Down's syndrome, Alzheimer's disease, senile dementia . . . were there any other dementias that were viewed as being related to Alzheimer's Disease as of 1986? . . . . A: Again from a – in terms of the amyloid pathology, those would have been the only ones that were recognized at the time."). Thus, in contrast to Defendants' Dr. Levey, Dr. Cummings's testimony concerning the term "Alzheimer's disease and related dementias" is consistent with the intrinsic evidence his expert reports and deposition testimony.

Finally, Defendants' argument that "related dementias" could include any disease that shares symptoms with Alzheimer's disease defies common sense. For example, memory loss is common to those suffering from alcoholism, but surely Defendants would not suggest that

Dr. Davis's invention would extend to the use of galantamine to treat that disease. In any event, Defendants' view that "related dementias" are dementias that share symptoms with Alzheimer's disease rather than its neuropathology was rejected in the prosecution history and cannot be resurrected here. Accordingly, this Court should adopt Plaintiffs' proposed construction of "Alzheimer's disease and related dementias" as set forth in their portion of the JCCC.

B. "A Patient Suffering from Such a Disease"

While the parties agree that this disputed term encompasses humans, Plaintiffs contend that this term is limited to humans, whereas Defendants ask the Court to expand its meaning to any mammal – presumably encompassing the more than 5,400 known species of mammals. JCCC at 2. However, by failing to identify any non-human mammal that suffers from Alzheimer's disease,[9] Defendants have not properly placed this term in dispute. Moreover, Defendants fail to identify any intrinsic or extrinsic evidence that supports their position that the claim term "patient" extends to all mammals. To the extent they cite such evidence, they flagrantly misrepresent it in their effort to seek an overly broad construction of the claim term. The Court should reject Defendants' attempt to obtain such an absurd result.

Defendants claim that "the inventor defined 'patient' to mean 'a mammal, including a human.'" Def. Br. at 15 (citing '318 Patent, Ex. 1 at 1:45-47). A review of that text reveals *no* such definition. While the passage cited by Defendants refers to a method of treating mammals, including humans, it contains no reference whatsoever to the word "patient," much less a definition of that word. Pl. Br. at Ex. A, '318 Patent at 1:45-47.

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9 **REDACTED**

Inconsistently, Defendants also argue that the specification "by implication" supports a definition of "patient" that includes all mammals simply because the word "mammal" appears in the Summary of Invention. *Microsoft Corp. v. Multi-Tech Sys., Inc.*, relied upon by Defendants in support of this argument (Def. Br. at 16), involved different claim construction issues and does not support their position. In that case, Multi-Tech (the patentee) sought to expand the scope of the claims to cover a transmission of data on a packet-switched network even though the invention summary made reference only to transmission over a telephone line. *Microsoft Corp. v. Multi-Tech Sys., Inc.*, 357 F.3d 1340, 1348-49 (Fed. Cir. 2004). The Court of Appeals for the Federal Circuit rejected this strategy, stating that because the narrower language of transmission by telephone line was not merely a preferred embodiment but rather the only embodiment in the invention summary, the patentee could not obtain a broader construction. *Id.* Thus, in *Microsoft*, the patentee's failure to include a network in the invention summary led to a construction that did not include network transmission.

In contrast to the situation in *Microsoft*, Defendants here claim that because the invention summary mentions a mammal that a claim term must be expanded beyond an embodiment also mentioned. *Microsoft* does not support that conclusion. Moreover, it is beyond cavil that a patentee can claim less than she discloses. *See Johnson & Johnston Assocs. Inc. v. R.E. Serv. Co., Inc.*, 285 F.3d 1046, 1052-53 (Fed. Cir. 2002); *Unique Concepts, Inc. v. Brown*, 939 F.2d 1158, 1562 (Fed. Cir. 1991); *United Chromium, Inc. v. Int'l Silver Co.*, 60 F.2d 913, 915 (2d Cir. 1932) ("[T]he patentee is . . . free to show that the claim covers only a part of what it might."). Dr. Davis was at liberty to include in the invention summary a broader disclosure (mammal) than she claimed (a human patient suffering from Alzheimer's disease). She was also at liberty to use different words in the patent claims and specification. *See*

Fujikawa v. Wattanasin, 93 F.3d 1559, 1570 (Fed. Cir. 1996) (disclosure need not contain *in haec verba* support for the patent claims). *Microsoft* would apply here only if Dr. Davis attempted to claim all mammals after having only identified human patients in her Summary of Invention.

Similarly, Defendants' reliance on the Code of Federal Regulations fails to advance their definition of "patient." Defendants, citing 37 C.F.R. § 1.73, erroneously argue that a patentee is *required* to claim the full scope of what is included in the Summary of Invention section, and according to Defendants, interpretation of claim scope must necessarily be of "commensurate" breadth. Def. Br. at 16-17. However, 37 C.F.R. § 1.73 makes clear that "any object [of the invention] recited should be that of the invention as claimed." Defendants' position overlooks the fact that the object of the invention of the '318 Patent is "to improve the cognitive function of patients with Alzheimer's disease," not to improve cognitive function in all mammals. *See* Pl. Br. at Ex. A, '318 Patent at 1:41-42.[10] In any event, the disclosure of an invention may be broader than the scope of the invention actually claimed. Any other rule would be unworkable because at the time a patent application is filed, the applicant cannot predict what narrowing claim amendments the PTO may require to avoid prior art, and as a result of this give-and-take, many claims cover less than the original disclosure.

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[10] Defendants cite the text in the '318 Patent (at 1:38-42) that refers to the need for "effective means of improving the functional status of *persons* with [Alzheimer's] disease" in arguing that because Dr. Davis used that term and "patients," they must have a different meaning. Def. Br. at n. 6. Defendants are correct to cite this passage, but have turned it on its head. This passage comes at the end of the Background Art section, and is followed immediately by: "It is an object of the present invention to improve the cognitive function of patients with Alzheimer's disease." Pl. Br. at Ex. A, '318 Patent at 1:38-42. Thus, after describing the problem *in humans* Dr. Davis identified the object of the invention, namely of solving *that problem* in human *patients*. The text relied upon by Defendants reveals that Dr. Davis used these terms synonymously, not differently.

Far from supporting Defendants' overly broad construction that "a patient suffering from such a disease" extends to any mammal, the '318 Patent file history instead confirms Plaintiffs' narrower definition of "patients." Defendants claim that Dr. Davis's September 11, 1986 Response (Pl. Br. at Ex. G) somehow reveals that Dr. Davis intended her invention to cover mice. This is sheer nonsense. Indeed, even the passage quoted by Defendants refers to her experiments "using [an] animal *model[]*" – *i.e.*, a model for testing drugs for human Alzheimer's disease. Def. Br. at 17 (emphasis added). Moreover, Defendants' unsupported suggestion to the contrary, animal models (involving mice or other animals) routinely serve as an initial step (to be followed by clinical testing) in development of drugs for human use. *See* 21 C.F.R. § 314.610 (permitting FDA to grant marketing approval for use of a drug in humans on the basis of animal studies that "establish that the drug product is reasonably likely to produce clinical benefit in humans."). In fact, the same paragraph from which Defendants quote reveals references by Dr. Davis to the "major and growing problem [or Alzheimer's disease] to our society" and the estimate of "over 1,000,000 sufferers of this disease in the United States alone." Pl. Br. at Ex. G, at 2. Clearly Dr. Davis was not expressing concern about an Alzheimer's epidemic in mice and the resulting costs to society.

The plain language of the patent also defeats Defendants' position that the reference to animal models somehow draws mammals into the scope of the patent claims. The patent refers to Dr. Davis's suggestion of a "test" that "provides a good animal model for Alzheimer's disease *in humans*...." Pl. Br. at Ex. A, '318 Patent at 2:45-46 (emphasis added). To one of ordinary skill in the art, the reference in the patent and in the file history to animal models for testing Alzheimer's disease drugs would confirm that the patients for whom therapy was intended was humans.

C. "Therapeutically Effective Amount"

As with their "construction" of "related dementias," Defendants have effectively declined to define "therapeutically effective amount," and merely paraphrase the claim language that it is "an amount sufficient to produce the desired therapeutic effect or change in a patient." JCCC at 2-3. This provides no help to the Court at all. In contrast, Plaintiffs' proposed construction specifies that the amount must be "sufficient to cause a therapeutically beneficial effect on the symptoms of Alzheimer's disease and related dementias." *Id.* And, as stated in Section A above, because cognitive impairment is the critical symptom of Alzheimer's disease, the "therapeutically effective amount" must be sufficient to treat that core symptom.

Nothing in the intrinsic evidence supports a construction that merely parrots the claim language. In contrast, Plaintiffs' construction finds ample support in the '318 Patent. *See, e.g.*, Pl. Br. at Ex. A, '318 Patent at 1:41-42 ("It is an object of the present invention to improve the cognitive function of patients with Alzheimer's disease"); *id.* at 1:48-50 (referring to a "cognitively enhancing amount of galantamine" or acid addition salt thereof). Indeed, the parties do not dispute that the "therapeutically effective amount" of galantamine must address cognitive function. Def Br. at 15.

D. "A Method of Treating [Alzheimer's Disease and Related Dementias]"

Because Defendants have offered a definition of this term appearing in the preamble of Claim 1, the parties agree that it should be defined by the Court. Plaintiffs' definition ("a method of alleviating the symptoms or deferring the decline associated with Alzheimer's disease, including the cognitive impairment that is the core symptom of the disease, in a manner beneficial to the patient – that is, in a manner that is safe, tolerable, and produces clinically meaningful results") finds ample support in the intrinsic evidence. Defendants' proposed definition ("administration of a drug product (*i.e.*, galantamine) to improve the

cognitive function or functional status of a patient with Alzheimer's disease or related dementias") does not. Def. Br. at 10. Defendants' definition differs from Plaintiffs' in three important respects: (1) it fails to require that alleviation of the core Alzheimer's symptom of cognitive impairment; (2) it fails to acknowledge that either alleviating symptoms or deferring the decline associated with Alzheimer's successfully treats the disease; and (3) it fails to require that the method be safe and tolerable, and produce clinically meaningful results. *Id.*; JCCC at 2.

1. Any method of treating Alzheimer's disease must address cognitive impairment.

Defendants' definition states, in relevant part, that the claimed method involves administering galantamine "for the purpose of trying to improve the cognitive function *or* functional status in patients with Alzheimer's disease...." Def. Br. at 10 (emphasis added). By use of the disjunctive, Defendants make clear that the claim can mean that galantamine can be used merely to enhance functional status without improving cognitive function. While Plaintiffs do not dispute that addressing non-cognitive symptoms of Alzheimer's disease (e.g., aggressive behavior) is useful, Plaintiffs disagree that doing so without addressing cognitive function – the core Alzheimer's symptom – amounts to a method of treating that disease in the context of the '318 Patent.

Defendants first resort to a dictionary definition, but they do not (and cannot) explain how that definition favors their proposed construction over Plaintiffs'. Indeed, as explained in section II.D.2 below, Defendants' dictionary definition of "treatment" supports *Plaintiffs'* construction.

Likewise, the intrinsic evidence Defendants cite supports *Plaintiffs'* construction. Specifically, Defendants cite two passages from the '318 Patent, which state:

> At present there is *no effective means of improving the functional status of persons with the disease*. It is an object of the present invention *to improve*

> *the cognitive function* of patients with Alzheimer's disease. (Def. Br. at Ex. 1, 1:38-42 (emphasis added.))
>
> A method for treating Alzheimer's disease and related dementias which comprises administering to mammals, including humans, an effective Alzheimer's disease *cognitively-enhancing* amount of galantamine...." (*Id.* at 1:45-48 (emphasis added)).

Def. Br. at 10-11 (emphasis in original).[11] As to the first quotation, the first sentence makes clear that Dr. Davis is referring generally to the problem her invention intends to address, namely, improving the functional status in Alzheimer's patients. The second sentence (the object of the invention) identifies the cause of that problem that she intends to solve – namely, the decline in cognitive function in Alzheimer's patients. In the second quotation (coming directly after the first in the '318 Patent), Dr. Davis identifies her solution: administering to Alzheimer's patients a "cognitively-enhancing" amount of galantamine. There can thus be no doubt that Dr. Davis made clear that her method treating Alzheimer's disease is directed to addressing the core symptom of cognitive impairment (via administration of galantamine) rather merely than to other functional deficits that result from the disease.

2. Alzheimer's disease can be meaningfully treated either by alleviating symptoms or deferring the decline of the disease.

Defendants also dispute Plaintiffs' construction insofar as it specifies that Dr. Davis's claimed method of treating Alzheimer's disease can involve either alleviating symptoms (of cognitive impairment, as shown above) or defer the decline associated with the disease. As for alleviating the symptoms, Defendants' claim that Plaintiffs have been "hopelessly vague" rings hollow. Def. Br. at 12. Plaintiffs do not, as Defendants contend, "mean that 'treating' extends to amelioration of symptoms beyond cognitive or functional, such as behavioral

[11] In their respective opening briefs, both parties rely on these same passages from the '318 Patent. *Compare* Pl. Br. at 10 and Def. Br. at 10-11.

symptoms." *Id.* To the contrary, Plaintiffs' construction (in the JCCC and Plaintiffs' Brief) narrowly targets cognitive decline as the core symptom that must be addressed. That Dr. Davis's invention may treat symptoms *in addition to* cognitive decline does not detract from the focus of her claimed method on that symptom.

Likewise, Defendants' professed confusion about what Plaintiffs mean by "deferring the decline of [Alzheimer's] disease" should be viewed with skepticism. Indeed, the dictionary definition offered by Defendants supports its inclusion in Plaintiffs' construction. In that definition, Defendants state that "'treating' ... is used to describe 'any specific procedure for the cure or the amelioration of a disease or pathological condition.'" Def. Br. at 10 (quoting Taber's Cyclopedic Medical Dictionary, 18th ed., p. 1990 (2005)).[12] It is undisputed that Alzheimer's disease involves the gradual deterioration of intellect, memory, and cognition. *See*

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; Ex. M, Second Expert Report of Dr. Murray A. Raskind at ¶ 15. It stands to reason that a treatment (such as Dr. Davis's invention) that helps to preserve cognition in Alzheimer's patients will defer the decline associated with the disease. Thus, each of the patent's references to improving or enhancing cognition (cited above) repudiate Defendants' claim that the intrinsic evidence does not support Plaintiffs' construction. Def. Br. at 12.

3. *A successful Alzheimer's treatment must be safe, tolerable, and produce clinically meaningful results.*

Accusing Plaintiffs of injecting "complex, largely commercial requirements" into their interpretation of this disputed claim term, Defendants reject Plaintiffs' contention that the

[12] Plaintiffs note that Defendants cite a 2005 dictionary in support of their construction of what one of skill in the art would have understood the '318 Patent claims to mean in 1986.

claimed method is of a treatment that is safe, tolerable, and produces clinically meaningful results. Def. Br. at 1, 13; JCCC at 2. But the '318 Patent and its file history contain several references that make clear the need for a safe and tolerable treatment, such as, for example:

- Pl. Br. at Ex. A, '318 Patent at 1:64-66 ("It may be necessary to begin at lower doses than are ultimately effective" – *i.e.*, titrating up to a safe and effective dose for a patient);[13]
- *Id.* at 2:67-3:3 ("There have been reports that galanthamine can cause cardiac arrhythmias. In such cases, it may be desirable to administer galanthamine in conjunction with another drug such as propanthelinbromide to control such arrhythmias");
- Pl. Br. at Ex. G at 2 (in which Dr. Davis informs the PTO that the "poor therapeutic index" of physostigmine – another cholinesterase inhibitor – is "likely to preclude its widespread use" and thus "there is no generally effective [Alzheimer's disease] treatment available");[14] and
- *Id.* ("... [G]alanthamine is currently being used in Europe to assist in the post-operative recovery from anesthesia and so is unlikely to suffer the problems of possible toxicity encountered with physostigmine" (citation omitted)).

Thus, placing the disputed claim term in the context of the overall invention (namely, an Alzheimer's treatment) and reviewing the intrinsic evidence should allay any doubt that a safe, tolerable, and effective treatment was what Dr. Davis invented. The patent and file history reveal that one of ordinary skill in the art in 1986 would have known of the association of adverse side effects with cholinesterase inhibitors (like physostigmine), which Dr. Davis expressly distinguished from her safer galantamine invention.[15]

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14 **REDACTED**

15 In their brief, Defendants selectively quote from the references in the file history to physostigmine as "effective in treating Alzheimer's disease," and conclude that Plaintiffs' construction "is designed to avoid prior art...." Def. Br. at n. 4. Defendants' citation to the file (continued...)

Defendants make much of three patents that expressly specify safety in addition to therapeutic efficacy (two of which issued long after the '318 Patent). Def. Br. at 14. These patents shed no light on claim construction here, and moreover courts have construed the claim term "effective" in the pharmaceutical context as encompassing a safety requirement. *See, e.g., Purdue Pharma. L.P. v. F.H. Faulding & Co.*, 48 F. Supp. 2d 420,437 (D. Del. 1999), *aff'd*, 230 F.3d 1320 (Fed. Cir. 2000) (construing "effective to treat pain" to mean "an individual patient is provided with adequate pain relief without unacceptable side effects").

Defendants thus contend that Dr. Davis's use of galantamine to treat Alzheimer's disease need not be safe and tolerable, nor provide clinically meaningful results. This simply makes no sense and is contradicted by Defendants' actions. As the Court is aware, Defendants have *conceded* infringement. Presumably Defendants would not dispute that their infringing products would provide Alzheimer's patients with a safe, tolerable, and clinically meaningful treatment for Alzheimer's disease.

III. CONCLUSION

For the reasons set forth above and in their Opening Brief, Plaintiffs respectfully request that the Court adopt Plaintiffs' proposed constructions of the disputed claim terms of the '318 Patent set forth in their portion of the JCCC.

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history is misleading because they fail to note that in her Sept. 11, 1986 Response to an Office Action, Dr. Davis *expressly distinguished* her galantamine invention from physostigmine which had an unsafe "therapeutic index." Pl. Br. at Ex. G at 2. Thus, the portion of the file history that Defendants rely upon for their alleged invalidity case supports a construction, offered here by Plaintiffs, that undermines their case. Plaintiffs further note that in response to Dr. Davis's Sept. 11, 1986 Response, the PTO issued a Notice of Allowability. *See* Ex. R (JAN-RAZ 0000040).

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